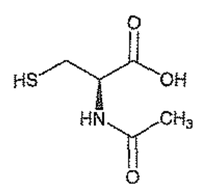
Acetylcysteine



$C_5H_9NO_3S$ 163.19
L-Cysteine, *N*-acetyl-;
N-Acetyl-L-cysteine [616-91-1].

DEFINITION
Acetylcysteine contains NLT 98.0% and NMT 102.0% of $C_5H_9NO_3S$, calculated on the dried basis.

IDENTIFICATION
• **A. Infrared Absorption** ⟨197K⟩

ASSAY
• **Procedure**

Mobile phase: 6.8 g/L of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 3.0.

Sodium metabisulfite solution: 0.5 mg/mL of sodium metabisulfite in water, freshly prepared

Internal standard solution: 5 mg/mL of USP L-Phenylalanine RS in *Sodium metabisulfite solution*

Standard stock solution: 10 mg/mL of USP Acetylcysteine RS in *Sodium metabisulfite solution*

Standard solution: 0.5 mg/mL of USP Acetylcysteine RS and 0.25 mg/mL of USP L-Phenylalanine RS in *Sodium metabisulfite solution* from *Standard stock solution* and *Internal standard solution*

Sample stock solution: 10 mg/mL of Acetylcysteine in *Sodium metabisulfite solution*

Sample solution: 0.5 mg/mL of Acetylcysteine and 0.25 mg/mL of USP L-Phenylalanine RS in *Sodium metabisulfite solution* from *Sample stock solution* and *Internal standard solution*

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 214 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection size: 5 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for acetylcysteine and L-phenylalanine are about 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6 between acetylcysteine and L-phenylalanine

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of acetylcysteine ($C_5H_9NO_3S$) in the portion of Acetylcysteine taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of acetylcysteine to L-phenylalanine from the *Sample solution*
R_S = peak response ratio of acetylcysteine to L-phenylalanine from the *Standard solution*
C_S = concentration of USP Acetylcysteine RS in the *Standard solution* (mg/mL)
C_U = concentration of acetylcysteine in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES
• **Residue on Ignition** ⟨281⟩: NMT 0.5%

Delete the following:

•• **Heavy Metals**, *Method II* ⟨231⟩
[CAUTION—Exercise care because explosion may occur.]
Analysis: In a dropwise manner, wet the sample with 2 mL of nitric acid, and proceed as directed for the *Test preparation*.
Acceptance criteria: NMT 10 ppm •• (Official 1-Jan-2018)

SPECIFIC TESTS
• **Optical Rotation**, *Specific Rotation* ⟨781S⟩

Buffer: Mix 29.5 mL of 1 N sodium hydroxide, 50 mL of 1 M monobasic potassium phosphate, and sufficient water to make 100 mL. Adjust to a pH of 7.0 ± 0.1 by adding more of either solution, as necessary.

Sample solution: In a 25-mL volumetric flask, mix 1.25 g with 1 mL of edetate disodium solution (1 in 100), add 7.5 mL of sodium hydroxide solution (1 in 25), and mix to dissolve. Dilute with *Buffer* to volume.

Acceptance criteria: +21° to +27°

• **pH** ⟨791⟩: 2.0–2.8 in a solution (1 in 100)

• **Loss on Drying** ⟨731⟩: Dry a sample at a pressure of about 50 mm of mercury at 70° for 4 h: it loses NMT 1.0% of its weight.

ADDITIONAL REQUIREMENTS
• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩
USP Acetylcysteine RS
USP L-Phenylalanine RS

Acetylcysteine Solution

DEFINITION
Acetylcysteine Solution is a sterile solution of Acetylcysteine in water, prepared with the aid of Sodium Hydroxide. It contains NLT 90.0% and NMT 110.0% of the labeled amount of acetylcysteine ($C_5H_9NO_3S$).

IDENTIFICATION
• **A. Infrared Absorption** ⟨197K⟩

Sample solution: Place 10 mL in a suitable beaker, and adjust to a pH of 2 (pH indicator paper), using 3 N hydrochloric acid. Add up to 2 g of finely powdered sodium chloride, in two portions of 200 mg each initially and then in smaller portions of 25 mg, stirring after each addition until the sodium chloride dissolves and a precipitate is formed. The precipitate appears as a very fine powder, and the solution turns cloudy. If no precipitate forms, add an additional drop of 3 N hydrochloric acid, and stir until the precipitate forms. Allow to stand at room temperature for 15 min, and collect the residue by suction filtration. Use the acetylcysteine so obtained after being dried at a pressure of 50 mm of mercury at 70° for 4 h.

Acceptance criteria: Meets the requirements

ASSAY

Change to read:

• **Procedure**

Solution A: 0.5 mg/mL of sodium metabisulfite solution in water, freshly prepared